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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,503	02/16/2006	Hye-Kyung Chang	1599-0315PUS1	3511

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EXAMINER	
SHTERENGARTS, SAMANTHA L	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
10/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,503	CHANG ET AL.	
	Examiner	Art Unit	
	Samantha L. Shterengarts	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-11* is/are allowed.

6)☒ Claim(s) *12-21* is/are rejected.

7)☒ Claim(s) *13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *16 February 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. The instant application is a national stage entry of PCT/KR04/02139, filed August 26, 2004, which claims foreign priority to Korean Application No. 10-2003-0059451, filed August 27, 2003.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on February 16, 2006 in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS document was considered. A signed copy of form 1449 is enclosed herewith.

Election/Restrictions

3. Applicant's election with traverse of Group II in the reply filed on September 3, 2008, is acknowledged. Although the traversal has not been found persuasive, upon further consideration, Examiner has decided to withdraw restriction and election of species requirements. Claims 1-21 will be examined on their merits.

Claim Objections

4. Claim 13 is objected to because of the following informalities: One of the diseases appears to be misnamed. It appears that "cerebral injure by hepatitis" should be "cerebral injuries (or injury) by hepatitis." Appropriate correction is required.

Claim Rejections - 35 USC § 112

(First Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 12-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of apoptosis, does not reasonably provide enablement for prevention of inflammation, and treatment of dementia, cerebral stroke, brain impairment due to AIDS, diabetes, gastric ulcer, cerebral injury by hepatitis, hepatitis-induced hepatic diseases, acute hepatitis, fulminant hepatic failure, liver cirrhosis, sepsis, organ transplantation rejection, and rheumatic arthritis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The Nature of the Invention

Claims 12-20 are drawn to a therapeutic composition for preventing inflammation and apoptosis comprising the caspase inhibitor compound of formula (I), salt, or stereoisomer thereof; the composition for treatment of dementia, cerebral stroke, brain impairment due to AIDS, diabetes, gastric ulcer, cerebral injury by hepatitis, hepatitis-induced hepatic diseases, acute hepatitis, fulminant hepatic failure, liver cirrhosis, sepsis, organ transplantation rejection, rheumatic arthritis, or cardiac cell apoptosis due to ischemic cardiac diseases; a process for preparing the therapeutic composition for preventing inflammation and apoptosis; and, a method for preventing inflammation and apoptosis.

The prophylactic treatment or "prevention" actually means to anticipate or counter in advanced, to keep from happening, etc. and there is no disclosure as to how one skilled in the art

can reasonably establish the basis and the type of subject to which the instant compounds, compositions, and medicaments can be administered in order to have the "preventative" effect.

The State of the Prior Art and the Predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instantly claimed invention is highly unpredictable as discussed below: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic and preventive effects of the above listed diseases, whether or not the disease is affected by the instantly claimed compounds.

With regards to products for the treatment and prevention of cognitive disorders, there are various classifications for all cognitive disorders. One of the claimed disorders, dementia, as defined by Medline Plus, is word for a group of symptoms caused by disorders that affect the brain. It is not a specific disease. Right now, dementia related diseases are not preventable. In terms of attention deficit disorder, Medline Plus discussed how "No one knows exactly what

causes ADHD." One of ordinary skill in the art cannot be enabled to treat and prevent this disorder when there is not a known cause.

www.nlm.nih.gov/medlineplus/dementia.html#cat5

Stroke represents one of the intractable medical challenges. Stroke is estimated to cause about 15% of deaths. Even those who survive them normally suffer from persistent damage, including motor and speech disturbances and/or convulsions. Despite a tremendous effort to resolve these problems, cerebrovascular therapy has so far been limited to trying to prevent further damage in areas on the margins of the ischemic focus, thus trying to maintain adequate perfusion in remaining intact areas, and thereby limit progressive infarction. This is generally done surgically. Standard pharmaceutical treatments, such as antiarrhythmics and antithrombotics, don't get at the cause of the stroke or the damage caused, but are mostly administered to insure adequate cardiac functioning.

With regards to methods of treating and preventing inflammatory disorders, the diseases are too divergent and require different methods of treatment. Examples of disorder associated with inflammation include, but are not limited to: asthma, autoimmune diseases, chronic inflammation, chronic prostatitis, glomerulonephritis, hypersensitivies, inflammatory bowel diseases, pelvic inflammatory disease, reperfusion injury, rheumatoid arthritis, shoulder tendonitis, transplant rejection, vasculitis, and various allergies. This broad list of diseases each has a different cause, and for the majority of the list, a different treatment. There is not one class of compounds, let alone one compound, which can treat/prevent all of these diseases.

For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually in any part of the

body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Accordingly, treatments for inflammation can normally be tailored to the particular type of inflammation present, as there is no, and there can be no, "magic bullet" against inflammation generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilation and leaking of vessels. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. There are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. This discussion, demonstrates the extraordinary breadth of the causes, mechanisms, and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to accept any agent for treatment and prevention of inflammation generally. For example, rheumatoid arthritis remains a clinical entity of unknown etiology, Gripenberg, pg. 85. (Gripenberg, M, Scand. J. Rheumatology, Vol. 10 (2) 1981, 85-91). Applicant's disclosure does not enable one of ordinary skill in the art to make or use the claimed invention within the entire scope of the diseases listed above. The diseases exemplified above do not encompass the entire list of non-enabled diseases, they are merely

examples to show the lack of enablement herein. There is no compound, let alone entire classes of compounds, that can reverse, alleviate, prolong the progression of, prevent, or treat the various and divergent diseases listed above, as claimed.

The Amount of Direction / Guidance Present and the Presence or Absence of Working Examples

The only direction or guidance present in the instant specification is the listing of diseases, as well as the guidance present for treatment of apoptosis. The specification does not contain any evidentiary support that these caspase inhibitors, or their obvious variants, would be able to treat and prevent the plethora of diseases listed. Furthermore, there are no working examples to support the treatment and/or prevention of the instantly claimed disorders.

The breadth of the claims

The claims are drawn to a method of treating and preventing the list of diseases as claimed in instant claims 12 thru 15. Note one compound, let alone a genus of compounds, could possibly be effective for the prevention (reversal, alleviation, prolongation, progression) and treatment of all of the instantly claimed diseases.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the inventions is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compound exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the

compound of the instant claims for the treatment or prevention of the various diseases, as a result necessitating one of skill to perform an exhaustive search for which diseases can be treated or prevented by what compounds of the instant claims in order to practice the claimed invention. Only a majority of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not mean that the other diseases meet the enablement requirements.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases, out of all diseases, would be benefited (treated or prevented) by the compounds and compositions of Formula 1 and would furthermore have to determine which of the claimed compounds would provide treatment or prevention of which disease.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated or prevented by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting the diseases that are not enabled within the method claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 21 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 21 is drawn to the use of the caspase inhibitor compound of formula (1), salt, or stereoisomer thereof, as defined in claim 1, for preventing inflammation and apoptosis. It is unclear what method/process Applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active steps delimiting how this use is actually practiced.

Claims 21 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See, for example, *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner,* 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 21 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Allowable Subject Matter

7. Claims 1-11 are allowed over the prior art of record.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samantha Shterengarts whose telephone number is (571)270-5316. The examiner can normally be reached on Monday thru Thursday 9-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samantha L. Shterengarts/
Examiner, Art Unit 1626

/Kamal A Saeed, Ph.D./
Primary Examiner, Art Unit 1626